Effective Health Care

Pediatric Multiple Organ Dysfunction Syndrome

Results of Topic Selection Process & Next Steps

The nominator, the Pediatric Organ Dysfunction Information Update Mandate (PODIUM), is interested in a new AHRQ systematic review examining the performance characteristics of both clinical assessments and scoring tools in predicting outcomes among children with individual and multiple organ dysfunction. Due to limited program resources, the program will not develop a review at this time. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Pediatric Multiple Organ Dysfunction Syndrome (MODS)

Topic #: 0663

Nomination Date: April 18, 2016

Topic Brief Date: January 30, 2017

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Summary of Key Findings:

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new review on this topic would not duplicate existing efforts. We identified no completed or in-process reviews on the performance characteristics of scoring tools or clinical assessments for single organ dysfunction (KQ1) or scoring tools for multiple organ dysfunction (KQ2) in pediatric populations.
- Impact: A new evidence review has high impact potential, as the standard for care for assessing children with single and multiple organ dysfunction is unclear.
- Feasibility: A new review on this topic is feasible.
    - *Size/scope of review:* We identified a total of 65 studies pertaining to the key questions: 43 studies on the performance characteristics of clinical assessments and scoring tools for individual organ dysfunction (KQ1) and 22 studies on scoring tools for multiple organ dysfunction (KQ2).
    - *Clinicaltrials.gov:* We identified 2 studies potentially relevant to the key questions that are currently recruiting participants. However, both studies are among both adult and pediatric patients.

- Value: It is unclear what the value of a new evidence review would be. Although the nominator plans to develop a contemporary definition for pediatric MODS and establish a set of common data elements based on the results of a systematic review, other plans for use of a new systematic review, dissemination, or other evidence-based products such as a guideline and recommendations are unknown.

Table of Contents

Introduction

Each year in the U.S., approximately 200,000 children are admitted to Pediatric Intensive Care Units (PICUs).[1] Multiple Organ Dysfunction Syndrome (MODS), typically defined as the failure of more than one organ system, is a poorly understood entity that accounts for 18% of PICU admission diagnoses and is present in the majority of children who die in the PICU.[2] Although there are multiple pediatric severity of illness scores that estimate the risk of mortality in critically ill children, their performance characteristics have not been well described. As a result, there is considerable variation in the use of severity of illness tools in PICUs, and a lack of clarity on the definition of Pediatric MODS itself.

Topic nomination *#0663 Pediatric Multiple Organ Dysfunction Syndrome (MODS)* was received on April 18, 2016. It was nominated by the Pediatric Organ Dysfunction Information Update Mandate (PODIUM). We met with the nominator to discuss narrowing the proposed scope to be an appropriate size for an AHRQ review. The nominator decided to focus the proposed review on the performance characteristics of scoring tools and clinical assessments for 10 major organ systems, as well as the performance characteristics of scoring tools for MODS. The questions for this nomination are:

Key Questions*

Key Question 1. What are the performance characteristics of currently used scoring tools and clinical assessments to screen for single organ dysfunction in critically ill children?

a. Neurologic
   - Glasgow Coma Score, pupillary reaction
   - PCPC
   - Delirium (eg, CAPD and P-CAM)
b. Respiratory
   - PaO_2 to fraction of inspired oxygen (PaO_2/FiO_2 or P/F) ratio
   - SaO_2 to fraction of inspired oxygen (SaO_2/FiO_2) ratio
   - SpO2 to fraction of inspired oxygen (SpO2/FiO2) ratio
   - Oxygenation index (mean airway pressure x fraction of inspired oxygen x 100)/PaO_2)
   - Oxygen saturation index (mean airway pressure x fraction of inspired oxygen x 100)/oximetry saturation)
c. Cardiovascular
   - Heart rate, systolic and/or diastolic blood pressure, vasoactive-inotropic score, plasma biomarkers (troponin, BNP)
d. Gastrointestinal & Hepatic
   - AST, ALT, bilirubin, serum ammonia, albumin, prothrombin time (PT)/international normalized ratio (INR)
e. Renal
   - Continual renal replacement therapy
   - Acute kidney injury scores: pRIFLE, AKIN, KDIGO
f. Hematologic
   - White blood cell count (white blood cell count, lymphocyte count); platelet count (thrombocytopenia); hemoglobin/hematocrit (red cell distribution index, free hemoglobin, haptoglobin – anemia, hemolysis)
g. Coagulation
   - Coagulation abnormalities: PT, INR, aPTT, fibrinogen, antithrombin, TEG, ROTEM, d-dimers, platelet aggregometry
   - ADAMTS 13 concentration
h. Endocrine

- Blood concentration of glucose
- Blood concentration of cortisol
- Blood concentration of thyroxin & thriiodothyroxine

i. Immunologic
- HLA-DR expression on circulating mononuclear cells
- *ex vivo* whole blood production of TNFα following LPS stimulation
- Serum cytokine (e.g., IL-10) concentration

j. Endothelia
- Angiopoietin I, II
- Proteins S, C

Key Question 2: What are the performance characteristics of currently used scoring tools to screen for multiple organ dysfunction syndrome?

a. P-MODS
b. PIM
c. PRISM
d. PELOD

*Note: See *Abbreviations* under Table 1 for clarification on abbreviations above.

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, and outcomes, (PICOs) of interest. See Table 1.

Table 1. Key Questions and PICOTs

Key Questions	1. What are the performance characteristics of currently used scoring tools and clinical assessments to screen for single organ dysfunction in critically ill children?	2. What are the performance characteristics of currently used scoring tools to screen for multiple organ dysfunction in critically ill children?
Population	Critically ill children with single organ dysfunction, excluding critically ill premature infants (<36 weeks gestation)	Critically ill children with multiple organ dysfunction, excluding critically ill premature infants (<36 weeks gestation)
Interventions	a. Neurologic • Glasgow Coma Score, pupillary reaction • PCPC • Delirium (eg, CAPD and P-CAM) b. Respiratory • PaO_2 to fraction of inspired oxygen (PaO_2/FiO_2 or P/F) ratio • SaO_2 to fraction of inspired oxygen (SaO_2/FiO_2) ratio • SpO2 to fraction of inspired oxygen (SpO2/FiO2) ratio • Oxygenation index (mean airway pressure x fraction of inspired oxygen x 100)/PaO_2) • Oxygen saturation index (mean airway pressure x fraction of inspired oxygen x 100)/oximetry saturation) c. Cardiovascular • Heart rate, systolic and/or diastolic blood pressure, vasoactive-inotropic score, plasma biomarkers (troponin, BNP) d. Gastrointestinal & Hepatic • AST, ALT, bilirubin, serum ammonia, albumin, prothrombin time (PT)/international normalized ratio (INR) e. Renal • Continual renal replacement therapy • Acute kidney injury scores: pRIFLE, AKIN, KDIGO f. Hematologic • White blood cell count (white blood cell count, lymphocyte count); platelet count (thrombocytopenia); hemoglobin/hematocrit (red cell distribution index, free hemoglobin, haptoglobin – anemia, hemolysis) g. Coagulation • Coagulation abnormalities: PT, INR, aPTT, fibrinogen, antithrombin, TEG, ROTEM, d-dimers, platelet aggregometry • ADAMTS 13 concentration h. Endocrine • Blood concentration of glucose • Blood concentration of cortisol • Blood concentration of thyroxin & thriiodothyroxine i. Immunologic • HLA-DR expression on circulating mononuclear cells • *ex vivo* whole blood production of TNFα following LPS stimulation • Serum cytokine (e.g., IL-10) concentration	Multiple organ dysfunction scoring tools and severity of illness indicators: a. P-MODS b. PIM c. PRISM d. PELOD

	j. Endothelia • Angiopoietin I, II • Proteins S, C	
Comparators	Any comparator	Any comparator
Outcomes	Descriptive and predictive performance characteristics (accuracy [sensitivity and specificity], validity, reliability, discrimination, calibration, sensitivity to change, goodness of fit) for: • Mortality (eg, PICU mortality, 28-day mortality, hospital mortality, mortality post-discharge) • Functional outcomes/residual morbidity (eg, PCPC, POPC, FSS, WeeFIM, PEDI, cognitive [MSEL, WISC, BSID], adaptive [VABS)], diagnosis of depression, PTSD, or acute stress disorder) • Organ-specific outcomes/residual morbidity(eg, tracheostomy, gastric tube, continual renal replacement therapy) • Outcomes related to MODS (eg, duration of new or progressive MODS (NPMODS), composite time to complete organ dysfunction resolution) • Cost of medical care • Other patient-centered outcomes (eg, symptom improvement, quality of life [Health Utilities Index, PEDsQL, ITQOL, Children's Quality of Life-Child Form], duration of life, quality of dying, and effect of a patient's health care on loved ones)	Descriptive and predictive performance characteristics (accuracy [sensitivity and specificity], validity, reliability, discrimination, calibration, sensitivity to change, goodness of fit) for: • Mortality (eg, PICU mortality, 28-day mortality, hospital mortality, mortality post-discharge) • Functional outcomes/residual morbidity (eg, PCPC, POPC, FSS, WeeFIM, PEDI, cognitive (MSEL, WISC, BSID), adaptive (VABS), diagnosis of depression, PTSD, or acute stress disorder) • Organ-specific outcomes/residual morbidity (eg, tracheostomy, gastric tube, continual renal replacement therapy) • Outcomes related to MODS (eg, duration of new or progressive MODS (NPMODS), composite time to complete organ dysfunction resolution) • Cost of medical care • Other patient-centered outcomes (eg, symptom improvement, quality of life, duration of life, quality of dying, and effect of a patient's health care on loved ones)

Abbreviations: ADAMS= A Disintegrin And Metalloprotease with ThromboSpondin; AKIN= Acute Kidney Injury Network classification; ALT= Alanine Aminotransferase; APTT= Activated Partial Thromboplastin Time; AST= Aspartate Aminotransferase; BSID= Bayley Scales of Infant Development; BNP= B-type Natriuretic Peptide Blood Test; CAPD= Cornell Assessment of Pediatric Delirium; KDIGO= Kidney Disease Improving Global Outcomes classification system; FSS=Functional Status Score; INR= International Normalized Ratio; HLA-DR= Human Leukocyte Antigen - antigen D Related; ITQOL= Infant Toddler Quality of Life Measure; LPS= Lipopolysaccharides; MODS= Multiple Organ Dysfunction Syndrome; MSEL= Mullen Scales of Early Learning; NPMODS= New or Progressive Multiple Organ Dysfunction Syndrome; P-CAM= Pediatric Confusion Assessment Method; PEDI= Pediatric Evaluation of Disability Inventory; PICU= Pediatric Intensive Care Unit; PCPC= Pediatric Cerebral Performance Category; PEDsQL= Pediatric Quality of Life Inventory; PELOD= Pediatric Logistic Organ Dysfunction; PI= Pediatric Index of Mortality; P-MODS= Pediatric Multiple Organ Dysfunction Score; POPC= Pediatric Overall Performance Category; pRIFLE= Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease; PRISM=Pediatric Risk of Mortality; PT= Prothrombin Time; PTSD= Post-Traumatic Stress Disorder; ROTEM=thromboelastometry; TEG= thromboelastography; TNFα= Tumor necrosis factor alpha; VABS= Vineland Adaptive Behavior Scales; WeeFIM= Functional Independence Measure; WISC= Wechsler Intelligence Scale for Children

Methods

To assess topic nomination *#0663 Pediatric Multiple Organ Dysfunction Syndrome (MODS)* for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. " Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. " Establish the overall *importance* of a potential topic as representing a health or " healthcare issue in the United States. "
3. " Determine the *desirability of new evidence review* by examining whether a new " systematic review or other AHRQ product would be duplicative. "
4. " Assess the *potential impact* a new systematic review or other AHRQ product.
5. " Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. " Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Table 2 includes the citations for the reviews that were determined to address the key questions. Appendix B includes the list of the sources searched and potentially relevant titles identified by our research librarian.

Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether a new review could influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a literature search in PubMed from June 2011 to June 2016 and identified 327 unique articles. We reviewed all identified titles and abstracts for inclusion and classified identified studies by study design to assess the size and scope of a potential evidence review. We also included several studies suggested by the nominator that met our criteria. Lastly, we searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Table 2, Feasibility Column, Size/Scope of Review Section for the citations of included studies.

Value

We assessed the nomination for value (see Appendix A). We considered whether a partner organization could use the information from the proposed evidence review to facilitate evidence-based change; or the presence of clinical, consumer, or policymaking context that is amenable to evidence-based change..

Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

Results

Appropriateness and Importance

This is an appropriate and important topic. Approximately 200,000 children are admitted Pediatric Intensive Care Units (PICUs)[1] and 18% of those have Multiple Organ Dysfunction Syndrome (MODS) at admission.[2] A typical PICU admission costs nearly $17,000.[3]

Desirability of New Review/Duplication

A new evidence review on Pediatric MODS would not be duplicative of an existing product. We identified no completed or in process reviews on this topic.

Impact of a New Evidence Review

A new systematic review on Pediatric MODS may have high impact, as the standard for care for assessing children with single and multiple organ dysfunction is unclear.

Feasibility of a New Evidence Review

A new evidence review on Pediatric MODS is feasible. We identified a total of 65 studies pertaining to the key questions: 43 studies on the performance characteristics of clinical assessments and scoring tools for individual organ dysfunction[4-46] (KQ1) and 22 studies on scoring tools for multiple organ dysfunction[13,47-69] (KQ2). We also identified 2 studies[70,71] potentially relevant to the key questions that are currently recruiting participants. However, both studies are among both adult and pediatric patients.

See Table 2, Feasibility column for the citations that were determined to address the key questions.

Table 2. Key questions with the identified corresponding evidence reviews and original research

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing Original Research)
KQ 1a: Neurologic	None identified.	**Size/Scope of Review** Relevant Studies Identified: 9 • Prospective cohort: 4[4-6] • Retrospective cohort: 5[7-12] **ClinicalTrials.gov** None identified
KQ 1b: Respiratory	None identified.	**Size/Scope of Review** Relevant Studies Identified: 5 • Prospective cohort: 3[13-15] • Retrospective cohort: 2[16,17] **ClinicalTrials.gov** • None identified
KQ 1c: Cardiovascular	None identified.	**Size/Scope of Review** Relevant Studies Identified: 4 • Prospective cohort: 4[18-21] **ClinicalTrials.gov** None identified
KQ 1d: Gastrointestinal and Hepatic	None identified.	**Size/Scope of Review** Relevant Studies Identified: 5 • Prospective cohort: 3[22-24] • Retrospective cohort: 2[25,26] **ClinicalTrials.gov** None identified
KQ 1e: Renal	None identified.	**Size/Scope of Review** Relevant Studies Identified: 8

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing Original Research)
		• Prospective cohort: 4[27-30] • Retrospective cohort: 4[31-34] **ClinicalTrials.gov** • None identified
KQ 1f: Hematologic	None identified.	**Size/Scope of Review** Relevant Studies Identified: 4 • Retrospective cohort: 3[25,35-37] **ClinicalTrials.gov** • Recruiting: 1[70]
KQ 1g: Coagulation	None identified.	**Size/Scope of Review** Relevant Studies Identified: 4 • Prospective cohort: 1[38] • Retrospective cohort: 3[39-41] **ClinicalTrials.gov** None identified.
KQ 1h: Endocrine	None identified.	**Size/Scope of Review** Relevant Studies Identified: 2 • Prospective cohort: 2[42 24] **ClinicalTrials.gov** • None identified
KQ 1i: Immunologic	None identified.	**Size/Scope of Review** Relevant Studies Identified: 5 • Prospective cohort: 3[43-45] • Retrospective cohort: 2[25,46] **ClinicalTrials.gov** Recruiting: 1[71]
KQ 1j: Endothelia	None identified.	**Size/Scope of Review** None identified. **ClinicalTrials.gov** • None identified
KQ 2a: P-MODS	None identified.	**Size/Scope of Review** Relevant Studies Identified: 1 • Retrospective cohort: 1[47] **ClinicalTrials.gov** None identified
KQ 2b: PIM	None identified.	**Size/Scope of Review** Relevant Studies Identified: 14 • Prospective cohort: 9[13,48-55] • Retrospective cohort: 5[56-60] **ClinicalTrials.gov** None identified
KQ 2c: PRISM	None identified.	**Size/Scope of Review** Relevant Studies Identified: 5 • Prospective cohort: 3[61-63] • Retrospective cohort: 2[68,69] **ClinicalTrials.gov** None identified

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing Original Research)
KQ 2d: PELOD	None identified.	**Size/Scope of Review** Relevant Studies Identified: 5 • Prospective cohort: 4[63-66] • Retrospective cohort: 1[67] **ClinicalTrials.gov** None identified

Abbreviations: KQ=Key Question

Value

The potential for value of a new systematic review on Pediatric MODS is unclear. If this review was funded, the nominator would convene a consensus conference that would use a new review to 1) develop a contemporary definition for pediatric MODS and 2) establish a common set of data elements that will facilitate data sharing and help to develop future therapies. However, other plans for use of a new systematic review, dissemination, or other evidence-based products such as a guideline and recommendations are unknown.

Summary of Findings

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new review on this topic would not duplicate existing efforts. We identified no completed or in-process reviews on the performance characteristics of scoring tools or clinical assessments for single organ dysfunction (KQ1) or scoring tools for multiple organ dysfunction (KQ2) in pediatric populations.
- Impact: A new evidence review has high impact potential, as the standard for care for assessing children with single and multiple organ dysfunction is unclear.
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Appendices

Appendix A: Selection Criteria Summary (

Appendix B: Search Strategy & Results (Feasibility)

Appendix A. Selection Criteria Summary (

Selection Criteria	Supporting Data
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents a health care drug and intervention available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on performance characteristics of screening tools and tests.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes, the topic represents a significant disease burden. Approximately 200,000 children are admitted to Pediatric Intensive Care Units (PICUs)[1] and 18% of those have Multiple Organ Dysfunction Syndrome (MODS) at admission. [2]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, this topic affects heath care decisions for a large, vulnerable population.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, the use of accurate screening tools in assessing the severity of illness can help health care providers select the most appropriate treatment at the appropriate time, which could potentially enhance benefits and mitigate harms.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, a typical PICU admission costs nearly $17,000.[3]
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	A new evidence review would not be redundant. We identified no completed or in process reviews on this topic.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, the standard of care is unclear.

4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, the standard of care is unclear.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	Size/scope of review: We identified a total of 65 studies pertaining to the key questions: 43 studies on the performance characteristics of clinical assessments and scoring tools for individual organ dysfunction[4-46] (KQ1) and 22 studies on scoring tools for multiple organ dysfunction[13,47-69] (KQ2). Clinicaltrials.gov: We identified 2 studies[70,71] potentially relevant to the key questions that are currently recruiting participants. However, both studies are among both adult and pediatric patients.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, the topic exists within a clinical context that is amenable to evidence-based change.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Although the nominator plans to develop a contemporary definition for Pediatric MODS and establish a set of common data elements based on the results of a systematic review, further plans are unknown.

Abbreviations: KQ= Key Question; PICU=Pediatric Intensive Care Unit

Appendix B. Search Strategy & Results (Feasibility)

Topic: Pediatric Mods Date: June 3, 2016 Database Searched: MEDLINE (PubMed)	
Concept	Search String
Organ Dysfunction Score (Mesh)	"Organ Dysfunction Scores"[Mesh]
OR	
Organ Dysfunction Score (keywords)	(((Organ[Title] OR respiratory[Title] OR lung[Title] OR heart[Title] OR renal[Title] OR hepatic[Title] OR liver[Title] OR kidney[Title] OR venous[Title])) AND (dysfunction[Title] OR function[Title] OR Failure[Title] OR insufficiency[Title])) AND (score[Title] OR scores[Title] OR scale[Title] OR category[Title] OR method[Title] OR index[Title] OR assessment[Title] OR tool[Title] OR test[Title])
OR	
Organ Dysfunction Scores (named)	((((((((((Glasgow Coma Scale[Title]) OR Pediatric Cerebral Performance Category[Title]) OR Cornell Assessment of Pediatric Delirium[Title]) OR Pediatric Confusion Assessment Method[Title]) OR Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease[Title]) OR Kidney Injury Network[Title]) OR Kidney Disease Improving Global Outcomes[Title]) OR Pediatric Multiple Organ Dysfunction Score[Title]) OR Pediatric Index of Mortality[Title]) OR Pediatric Risk of Mortality[Title]) OR Pediatric Logistic Organ Dysfunction[Title]))
OR	
Organ Dysfunction (Mesh w/terms for measuring)	(((((("Multiple Organ Failure"[Mesh]) OR "Respiratory Insufficiency"[Mesh]) OR "Heart Failure"[Mesh]) OR "Renal Insufficiency"[Mesh]) OR "Hepatic Insufficiency"[Mesh]) OR "Venous Insufficiency"[Mesh])) AND ((((((("classification"[MeSH Subheading]) OR "Classification"[Mesh]) OR "Trauma Severity Indices"[Mesh]) OR "Blood Cell Count"[Mesh]) OR "Blood Coagulation Tests"[Mesh]) OR "Platelet Function Tests"[Mesh]) OR "Liver Function Tests"[Mesh])
AND	
Pediatric	(((child[Title] OR children[Title] OR pediatric*[Title]))) OR ((("Pediatrics"[Mesh] OR "Intensive Care Units, Pediatric"[Mesh] OR "Hospitals, Pediatric"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh])
NOT	
Editorials, Etc.	((((("Letter"[Publication Type]) OR "News"[Publication Type]) OR "Patient Education Handout"[Publication Type]) OR "Comment"[Publication Type]) OR "Editorial"[Publication Type])) OR "Newspaper Article"[Publication Type]
Limit to last 5 years, Human, English	Filters activated: published in the last 5 years, Humans, English.
N=327	
Systematic Review ***N=13***	Systematic [sb]

Randomized Controlled Trials ***N=72***	((((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])
Other ***N= 242***	

ClinicalTrials.gov was searched on August 24, 2016

8 studies found for: Organ Dysfunction Scores | **Recruiting** | Child | Studies received from 08/24/2011 to 08/24/2016
https://clinicaltrials.gov/ct2/results?term=Organ+Dysfunction+Scores&recr=Recruiting&type=&rslt=&age_v=&age=0&gndr=&cond=&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv_s=08%2F24%2F2011&rcv_e=08%2F24%2F2016&lup_s=&lup_e=

no studies found for: Organ Dysfunction Scores | **Active, not recruiting** | Child | Studies received from 08/24/2011 to 08/24/2016

2 studies found for: Organ Dysfunction Scores **| Completed** | Child | Studies received from 08/24/2011 to 08/24/2016
https://clinicaltrials.gov/ct2/results?term=Organ+Dysfunction+Scores&recr=Completed&type=&rslt=&age_v=&age=0&gndr=&cond=&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv_s=08%2F24%2F2011&rcv_e=08%2F24%2F2016&lup_s=&lup_e=